

# **Systematic assessment of adult patients' satisfaction with various eosinophilic oesophagitis therapies**

**Short title:** patients' satisfaction with EoE therapies

Ekaterina Safroneeva, PhD<sup>1\*</sup>, David Hafner, BMed<sup>1\*</sup>, Claudia E. Kuehni, MD, MPH<sup>1</sup>, Marcel Zwahlen, PhD<sup>1</sup>, Sven Trelle, MD<sup>2</sup>, Luc Biedermann, MD<sup>3</sup>, Thomas Greuter, MD<sup>3</sup>, Stephan Vavricka, MD<sup>3</sup>, Alex Straumann, MD<sup>3</sup>, Alain M. Schoepfer, MD<sup>4</sup>

\*equal contribution of first two authors

## **Affiliations:**

1 Institute of Social and Preventive Medicine, University of Bern, Switzerland

2 Clinical Trials Unit Bern, Institute of Social and Preventive Medicine, University of Bern, Switzerland

3 Division of Gastroenterology and Hepatology, University Hospital Zurich, Zurich, Switzerland

4 Division of Gastroenterology and Hepatology, Centre Hospitalier Universitaire Vaudois (CHUV), University of Lausanne, Lausanne, Switzerland

## **Correspondence address:**

Ekaterina Safroneeva, PhD

Institute of Social and Preventive Medicine

University of Bern

Mittelstrasse 43

CH-3012, Bern, Switzerland

Tel: +41 (0) 31 631 59 71

24 Email: [ekaterina.safroneeva@ispm.unibe.ch](mailto:ekaterina.safroneeva@ispm.unibe.ch)

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**ABSTRACT**

**Background and aims:** Treatment options for eosinophilic oesophagitis (EoE) patients include drugs (proton-pump inhibitors [PPI], swallowed topical corticosteroids [STC]), elimination diets, and dilation. Given the lack of data, we aimed to assess adult EoE patients' satisfaction with different EoE-specific treatment modalities.

**Patients and methods:** We evaluated therapy satisfaction recalled over a 12-month period using the validated "Treatment Satisfaction Questionnaire for Medication" (TSQM) that assesses effectiveness, side effects, convenience, and overall satisfaction. The score for each scale ranges from 0 (dissatisfied) to 100 (satisfied). To evaluate satisfaction with non-pharmacologic therapies the questionnaire was modified and debriefed in three focus groups. The final questionnaire was sent to 148 patients.

**Results:** Patient response rate was 74%. In the last 12 months, 24%, 75%, 19%, and 9% were treated with PPI, STC, elimination diet, and dilation, respectively. Patients identified the following considerations as important for therapy choice: effect on symptoms (89%), effect on oesophageal inflammation (76%), side effects (69%), and ease of use (58%). Patients found STC to be effective (83 points), convenient (83 points), and experienced no side-effects when using this therapy. When using STC alone (43%), overall patient satisfaction was high (86 points). Patients judged PPI to be most convenient (89 points), STC to be a bit less convenient (83 points), and diet to be most inconvenient (46 points) of three therapies examined.

**Conclusions:** Adult EoE patients consider both therapy effect on symptoms and oesophageal inflammation as important criteria, when choosing EoE therapy, and appear to be satisfied with use of STC.

Word count: 250

**Key words:** eosinophilic oesophagitis, patient satisfaction, patient governance, shared decision-making

## INTRODUCTION

Three types of therapies, namely drugs, diets, and dilation, are used to manage adult patients with eosinophilic oesophagitis (EoE).<sup>1,2</sup> The drug-based therapy with most randomized placebo-controlled trials-generated evidence of efficacy in EoE is swallowed topical corticosteroids (STC) in a form of either syrup (budesonide diluted in sucralose solution), powder (obtained from blisters of fluticasone propionate inhaler discus or budesonide capsules), or spray (fluticasone propionate oral aerosol inhaler).<sup>1</sup> STC are currently being used mostly off-label given that a formulation of budesonide developed specifically for adult EoE patients has only recently been approved by the European Medicines Agency (in 2017) and Swiss regulators (in 2018).<sup>3</sup> Proton-pump inhibitors (PPI) are used in a subset of EoE patients responsive to this medication or else in those suffering from concomitant gastro-oesophageal reflux disease.<sup>1</sup> Six-food (or less) elimination diet is a non-drug-based alternative for EoE management. Just like STC, the diet may lead to a reduction of oesophageal inflammation and symptomatic relief.<sup>1</sup> Lastly, dilation of strictures often results in symptom relief that may be long-lasting; however, this measure does not affect the inflammatory activity of the disease.<sup>1</sup> These therapy options are associated with either a risk of side effects, potential long-term sequelae associated with uncontrolled inflammation (dilation), or else need for a long-term avoidance of staple foods, such as milk, wheat and eggs (diet). As such, patients' perception of the efficacy and safety as well as life-style preferences may profoundly influences the choice of EoE-specific therapy.

To date, adult patients' satisfaction with various EoE-specific therapies has not been systematically assessed. The Treatment Satisfaction Questionnaire for Medication (TSQM) is a validated, general measure of patients' satisfaction with medication.<sup>4,5</sup> We used the questions of the TSQM as well as those specifically developed for the purposes of this study to perform a questionnaire-based survey. In this prospective survey study, we aimed to evaluate the utilization of various EoE-specific therapies, assess adult patients' satisfaction with the therapies they received in the last 12 months, and examine factors that are important for patients' choice of therapy.

## METHODS AND PATIENTS

An overview of the key steps described in the methods section is shown in **Figure 1**.

### Study population

Between September 2016 and November 2016, adult EoE patients ( $\geq 17$  years of age) were recruited in 1 ambulatory care clinic in Switzerland as a part of the Swiss EoE Cohort Study (SEECs). The study was approved by ethic committee of canton Vaud (CER-VD, protocol number 148/15).<sup>6</sup> Patients provided written informed consent for participation in the study. Disease diagnosis was established by investigators according to standardized criteria.<sup>1</sup> Patients with concomitant gastro-oesophageal reflux disease were also included.

### Development of the preliminary version of the study questionnaire

We first created the questionnaire querying various demographic and disease-specific characteristics, utilization of various EoE-specific therapies and patients' satisfaction with the therapies used in the last 12 months.

The initial questionnaire contained the following ten domains: socio-demographic characteristics (eight items), EoE-specific patient history (three items), presence of gastro-oesophageal reflux (one item), presence of atopic diseases (four items), five items on past and present EoE-specific therapy (including PPI, STC, systemic corticosteroids, diets, and dilation), and factors that are important for patients' choice of therapy (two items). In addition, the questionnaire contained validated items (questions) from TSQM that assesses treatment satisfaction with various therapies.<sup>4,5</sup> Patients were asked to think of the satisfaction with various therapies, when looking back at the 12-months period. The TSQM was previously translated into German and underwent cultural adaption for Switzerland (TSQM version 1). The validated TSQM covers the most relevant aspects of the patients' satisfaction with medication. The TSQM consists of 14 items falling into four scales: effectiveness (three items), side effects (five items), convenience (three items), and overall satisfaction (three items) (**Supplementary Table 1**).<sup>4,5</sup> Unlike many other similar measures, the TSQM may also be used to compare various patient conditions and medication types. Treatment Satisfaction Questionnaire for Medication scale was used five times in the initial

questionnaire (including PPI, STC, systemic corticosteroids, diet, and dilation). The TSQM scale scores range from 0 (indicates lack of effectiveness) to 100 (indicates excellent effectiveness).

### **Focus groups and individual patient interviews**

The focus group and individual patient interviews were conducted in accordance with ISPOR PRO Good Research Practices Task Force report.<sup>7,8</sup> The purpose of the focus groups was to aid in the item generation phase of questionnaire development and ensure that “respondents understand how to complete the questionnaire, how to reference the correct recall period, the meaning of the items, how to use the response scales, and any other questionnaire features that may influence patient responses in the intended mode of administration.”<sup>7,8</sup>

A board-certified psychologist (K.M., psychiatry clinic, University Hospital Basel) conducted two rounds of the cognitive interviews based on semi-structured interview guides that contained questions and probing strategies to assess patients' understanding of questions/probing strategies were also used to assess appropriateness of recall period. Lastly, content coverage, format, and length of the entire questionnaire were assessed. Each focus group lasted approximately two hours. Two facilitators were also present during the focus groups discussions (D.H., and either A.M.S. or A.S.). D.H. conducted 4 individual face-to-face semistructured interviews to find out, if last changes to the questionnaire had to be made. An individual patient interview lasted approximately 40 minutes. Focus groups/individual patient interviews were recorded, translated from Swiss dialect of German (not a written language) into German, and transcribed. The research team reviewed transcriptions of the focus groups.

Forty-five and six EoE patients were approached during a routine clinical visit in the EoE clinic (Olten, Switzerland) and invited to participate in the focus groups and the face-to-face patient interviews, respectively. Thirty-three and two patients declined the invitation in the focus groups and the face-to-face patient interviews, respectively. Twelve EoE patients were interviewed during two focus groups (n = 6 for each focus group). Of the six patients with mean age of 38.5 years (range 26-51) participating in focus group number one, two were

female. Of the six patients with mean age of 47.3 years (range 34-63) participating in focus group number two, one was female. Four male patients with mean age of 59.5 years [range 44-86] were individually interviewed.

We created semi-structured interview guides, which contained questions and probing strategies to assess patients' understanding of instructions, stem, response options and format of individual items. Depending on the item, questions/probing strategies were also used to assess appropriateness of recall period. Lastly, content coverage, format, and length of the entire questionnaire were assessed.

### **Final questionnaire**

We created a cognitive summary report and an item tracking matrix documenting all the changes that were made, which included the following ones: 1) a single item assessing the presence of atopic diseases was separated into 5 items; 2) the part about treatment satisfaction with STC was expanded to include three different forms of application, namely syrup, powder, and spray, as one participant of the focus group took the STC in two different formulations and was satisfied with one form of application, but not with another; and 3) several items querying the use of concomitant therapies was introduced.

The final questionnaire (**supplementary material**) consisted of the following 11 domains: socio-demographic characteristics (7 items), EoE-specific patient history (3 items), presence of reflux (1 item), presence of atopic diseases (4 items), concomitant therapies (including antacids, H2-receptor antagonists, PPI, and corticosteroids - 7 items), 5 items on past and present EoE-specific therapy (including PPI, STC, systemic corticosteroids, diets, and dilation), and factors that are important for patients' choice of therapy (2 items). The final questionnaire contains TSQM, which was used six times for assessment of satisfaction with PPI, STC (once per different application form - syrup, powder and spray), and dilation.<sup>4,5</sup> The final questionnaire also included the items of Eosinophilic Esophagitis Activity Index patient-reported outcomes (EEsAI PRO) questionnaire and adult EoE quality of life questionnaire (EoE-QoL-A).<sup>9,10</sup>

### **Changes to Treatment Satisfaction Questionnaire for Medication**



TSQM was developed for pharmacologic treatments and used in its original form for PPI and STC. Given the fact that some patients took PPI and/or STC for many years, “I don’t remember” response option to item three of TSQM (“time until the drug started working”) was introduced. TSQM was adapted for diet and dilation, for which not all TSQM items were applicable (for diet, the item on ease of use related to formulation was removed; for dilation, the entire convenience scale was removed). The word “medication” was replaced with either “diet” or “dilation” and complementary verb. (For reviewers only: The summary of the changes is shown in **Supplementary Table 2**).

### **Data handling and statistical analysis**

We double entered the data into EpiData (version 3.1, Denmark) database, compared our entries, and extracted the data into Stata (version 13, USA). Data were fairly complete, as only two missing responses were found for the lead in items that inquired whether the patient took STC in the last 12 months, and no missing values were found for PPI, diets, and dilation. For all therapy types, no values for any of the TSQM items were missing. Descriptive results are presented as frequencies and percentages of the group total or median, interquartile range, and range. Multivariable logistic regression modelling was performed to evaluate the potential factors that might be associated with the outcome “assigning most importance to effects of therapy on symptoms and oesophageal inflammation as opposed to symptoms alone”. The following variables were entered into the model as independent variables: age, female gender, disease duration, history of oesophageal dilation, history of endoscopic disimpaction, education level (presence of university education or equivalent<sup>11</sup>), and anti-inflammatory therapy at time of study participation (either individually or more than one therapy). In a first step, the potential associated factors were tested separately. In a second step, all factors with a P-value < 0.15 were entered together into the multivariable logistic regression model. To assess the possibility of effect modification, we evaluated pairwise interaction terms of predictor variables. A p-value < 0.05 was considered statistically significant.

## RESULTS

### Patient characteristics

The final version of the questionnaire was sent by mail to 147 adults with EoE. The survey response rate was 74% (108/147). Patient and disease characteristics are shown in **Table 1**. Mean patient age was 46.9 ( $\pm 5.3$ ) years, 85/108 patients (79%) were male, and mean disease duration was 7.6 ( $\pm 5.1$ ) years. At inclusion, 45%, 75%, and 19% were treated with PPI, STC, and food elimination diet, respectively. In the past 12 months, 10 patients underwent oesophageal dilation. Thirty-five patients (32%) were managed with more than one therapy (28 patients [26%] with more than one anti-inflammatory therapy). Ten patients (9.3%) did not receive any treatment.

### Satisfaction with therapy

TSQM scales scores as well as average TSQM values for PPI, STC, and diet are shown in **Table 2** (patients could be on more than one therapy in the past 12 months). When judging the convenience of using these EoE-specific therapies, patients found use of PPI being most convenient (score of 89). Although most patients needed to extract the steroid-powder containing blister from the diskus of asthma-specific medication, they found STC to be relatively convenient (score of 83). Patients on elimination diet found this therapy fairly inconvenient (score of 46). Patients did not observe any side-effects associated with the use of various EoE-specific therapies, which is consistent with their long-term use (especially PPI and STC, which were used for the duration of 6 and 5 years, respectively).

We also examined the therapy satisfaction in the population that used STC only (in a form of a powder), STC together with PPI, and STC together with elimination diets (**Table 3**). Patients found STC to be effective (score of 83), relatively convenient (score of 78), and experienced no side-effects when using this therapy. When using STC alone, overall satisfaction was fairly high (score of 86).

### Criteria important for the choice of therapy

The criteria that patients find important for the choice of therapy are shown in **Table 4**. The effect of therapy on symptoms (89%) and oesophageal inflammation (76%), possible side

effects (69%), and ease of therapy use (58%) were identified by patients as important considerations for the choice of therapy. When asked about the most important criterion for the choice of therapy (**Figure 2**), 45%, 32%, and 11% of patients chose the effect of treatment on symptoms and oesophageal inflammation, the effect of the treatment on the symptoms alone, and the effect of treatment on oesophageal inflammation alone, respectively, as deciding factor.

Step-wise logistic regression modelling was performed to identify factors associated with assigning most importance to improvement in symptoms and inflammation compared to that in symptoms alone as criteria for the choice of therapy (**Table 5**). In the univariable model, female gender, STC and PPI use at the time of the study were positively associated with putting greater emphasis on improvement in symptoms and oesophageal inflammation compared to that in symptoms alone, whereas presence of at least university degree (or equivalent) was negatively associated with this outcome. In the multivariable analysis, female gender (OR 3.727, 95%-CI 0.996-13.944, P-value=0.050), STC use at the time of the study (OR 3.760, 95%-CI 1.125-12.565, P-value=0.031), and PPI use at the time of the study (OR 2.911, 95%-CI 0.869-9.754, P-value=0.083) were positively associated with the outcome. In the multivariable analysis, we observed a trend for negative association between presence of at least university degree (or equivalent) and the outcome (OR 0.406, 95%-CI 0.148-1.117, P-value=0.081). We also carried out the regression modelling, in which the use of more than one anti-inflammatory therapy at the time of the study (as opposed to each therapy individually) was examined. We found that use of more than one anti-inflammatory therapy is positively associated with putting greater emphasis on improvement in symptoms and oesophageal inflammation compared to that in symptoms alone in both univariable (OR 6.544, 95%-CI 1.753-24.427, P-value=0.005) and multivariable analyses (OR 9.294, 95%-CI 2.309-37.405, P-value=0.002 for more than one anti-inflammatory therapy; OR 3.874, 95%-CI 1.061-14.152, P-value=0.040 for female gender; OR 0.385, 95%-CI 0.137-1.080, P-value=0.070 for presence of at least university degree).

## DISCUSSION

This is the first study that examines adult EoE patients' satisfaction with different therapies. We developed a survey to assess treatment satisfaction with EoE-specific therapy by consulting ISPOR guidelines and literature describing the use of TSQM as well as obtaining input from EoE patients by the means of focus groups and individual interviews. Patients with long-established EoE diagnosis appear to be satisfied with anti-inflammatory therapies, especially STC. We also found that effect of therapy on symptoms and oesophageal inflammation were important considerations for the choice of therapy in adults with EoE, and that female patients and those using anti-inflammatory therapies at the time of the study were more likely to assign greater importance to effect of therapy on both inflammation and symptoms as opposed to symptoms alone.

With an average TSQM score of 80, 85, 77 for PPI, STC and diet respectively, EoE patients appear to be satisfied with these EoE-specific therapies. Overall satisfaction scores as well as various TSQM scales scores are consistent with our current knowledge about these therapies. It is well known that whilst STC and diets appear to be efficacious/effective in the entire EoE patient population, PPI are only effective in a subset of EoE.<sup>12</sup> Hence, the effectiveness scores are higher for both STC and diet when compared to PPI. Although high side-effects scales scores are indicative of lack of therapy-related side-effects, it is more likely that these patients have been diagnosed with EoE for a relatively long time and would have had time to switch the therapy in case of side-effects. It is also not surprising that, PPI that are administered in a form of a tablet received the highest convenience score when compared to STC blister that needs to be extracted from the fluticasone discus inhaler developed for asthma patients and diets adhering to which require patients to cook their own meals. Given that many of the patients take the pharmacologic therapies for an extended period of time (median treatment duration of 5 years or longer), it is only fitting that overall relatively high satisfaction scores are observed, as both PPI, STC, and diets have proven efficacy/effectiveness in patients with oesophageal eosinophilia.<sup>12-14</sup> The overall satisfaction scores might have been different (and potentially lower), if therapy satisfaction would have

been evaluated in newly-diagnosed patients needing to decide on the type of therapy that would work best for them and encountering side-effects of these therapies.

When asked about considerations that are important for the therapy choice, adult EoE patients consider both effect of medication on symptoms and oesophageal inflammation as important. The finding that from patients' perspective therapy should target both inflammation and symptoms is consistent with the choice of endpoints for most recent trial testing short-term efficacy of STC in adults with EoE for the purposes of regulatory approval.<sup>15</sup> We found that female patients, those using single anti-inflammatory therapy, or a combination of those therapies at the time of the study were more likely to assign importance to effect of therapy on both symptoms and oesophageal inflammation as opposed to symptoms alone. Given that the majority of patients received a maintenance therapy of 0.25 mg of STC BID, a dose that brings only 16% of all patients into a complete remission, it is likely that disease activity in some of these patients on combination therapy was not adequately controlled.<sup>16,17</sup>

According to Atkinson *et al.* therapy satisfaction is a subset of overall patient satisfaction.<sup>4</sup> Besides therapy satisfaction, overall patient satisfaction covers all other "aspects of medical treatments, interpersonal aspects of clinical care, and processes of treatment".<sup>4</sup> Overall patient satisfaction interacts with the behaviour of patients as well as with the decision making. This relationship between overall patient satisfaction and patient's behaviour is not considered to be strictly causal in nature, but rather an interaction between the domains that can influence each other. For example, overall patient satisfaction (and therapy satisfaction) can influence patient's behaviour. We hypothesize that when an EoE patient is satisfied with the STC therapy (e.g. because of relative ease of use, effectiveness, or few side effects), it is more likely that this patient will pursue the treatment in a long-term run, even though most EoE symptoms would be gone following a short induction treatment. Given that EoE is a chronic disease, it is important for patients to adhere to anti-inflammatory treatment, as patients with an adequate disease control have fewer long-term complications, such as food bolus impactions.<sup>18</sup> It is also possible for patient's behaviour to influence therapy satisfaction. We hypothesize that an EoE patient, who is well-informed about advantages (e.g. no need

for medication) and disadvantages (e.g. may lead to lifestyle alterations) of dietary therapy for disease management is more likely to continue the therapy. As such, one could argue that minimizing the rates of therapy discontinuation through, among other things, better patient education might lead to a higher degree of satisfaction with EoE-specific therapy.

The results of this study should be interpreted with several considerations in mind. Although this is the first study that attempts to assess patients' satisfaction with various EoE-specific therapies, patients with long-established diagnosis from one gastroenterology practice specializing in management of this condition were recruited. It is likely that the high rates of therapy satisfaction might be a consequence of the following: 1) we ended up with a population of patients that used the therapies for a long time; and 2) it is likely that at least a proportion of patients, especially those participating in various clinical studies, were well informed about various aspects of this disease. As such, our results may not be generalizable to newly-diagnosed patients or those attending less-specialized gastroenterology practices. Whilst the patients' satisfaction with PPI and STC could be evaluated using the original form of the questionnaire, the questionnaire had to be adapted for diet and dilation. Although minor word changes were performed, or else non-applicable items were removed entirely, satisfaction with diet has been queried using a non-validated form of this questionnaire, and the data obtained should be interpreted with caution. Although we used a validated TSQM, it is important to point out that validity of the overall questionnaire has not been rigorously assessed. This is especially true of the items querying the importance of the effects of therapy on various aspects of the disease, as these were not evaluated against another valid questionnaire or construct. The rate of dietary treatment observed in this study is lower (19%) than that observed in centers specializing in elimination diets (up to 57% in mixed adult and paediatric population).<sup>19</sup> However, it is important to point out that the removal of inflammation-causing foods, such as milk- and wheat-based products, might pose challenges, as these foods represent important dietary staples of Swiss-German patients. Therefore, it is likely that, among other things, Swiss German patients' dietary and

361 physician's personal preferences contributed to high rates of STC use in the current  
362 population.

363 In conclusion, we found that patients with long-established EoE diagnosis appear to be  
364 satisfied with anti-inflammatory therapies, especially STC, and consider both symptoms and  
365 oesophageal inflammation as important targets for therapy.

## TABLES

**Table 1:** Characteristics of the survey's respondents.

Characteristics (n=108)	Frequency	%
Age at EoE diagnosis (years), mean $\pm$ SD	39.0 $\pm$ 15.6	NA
Age at inclusion (years), mean $\pm$ SD	46.9 $\pm$ 15.3	NA
Diagnostic delay (years), median (IQR), range	2.3 (0.3 - 9.3), 0 – 38.3	NA
Disease duration (years), mean $\pm$ SD	7.6 $\pm$ 5.1	NA
Symptom severity as assessed by EEsAI PRO score <sup>§</sup> , median, (IQR), range	12 (0 - 27), 0 - 65	NA
EoE-specific quality of life as assessed by EoE-QoL-A <sup>§§</sup> , median, (IQR), range	0.5 (0.29 – 0.96), 0 – 1.83	NA
Male gender	85	78.7
Family history of EoE	23	6.5
Nationality		
- Swiss	98	90.7
- Non-Swiss	10	9.3
ISCED 2011 education levels		
- Level 3	50	46.3
- Level 6 or higher	58	53.7
Experienced food bolus impaction that required endoscopic disimpaction (ever)	39	36.1
Gastrooesophageal reflux disease		
- Ever diagnosed	28	25.9
- Heartburn in last 7 days	29	26.9
Concomitant allergies (ever in life)		
- Asthma	37	34.3
- Allergic rhinitis	64	59.3
- Neurodermitis	27	25.0
- Known food allergies	42	38.9
- More than 1 condition	54	50.0
EoE-specific therapy		
- Swallowed topical corticosteroids (budesonide or fluticasone), ever	106	98.1
- Swallowed topical corticosteroids at inclusion	81	75.0
- Elimination diets, ever	27	25.0
- Elimination diets at inclusion	20	18.5
- Oesophageal dilation, ever	38	35.2
- Oesophageal dilation within last 12 months	10	9.3
Proton-pump inhibitor therapy		
- ever	49	45.4
- at inclusion	26	24.1

**Abbreviations:** EoE, eosinophilic oesophagitis; EEsAI PRO, eosinophilic oesophagitis activity index patient-reported outcome questionnaire; EoE-QoL-A, eosinophilic oesophagitis quality of life questionnaire for adults; IQR, interquartile range; NA, not applicable; SD, standard deviation; ISCED, international standard classification of education.<sup>21</sup>

<sup>§</sup>The EEsAI PRO questionnaire assesses symptom severity in adults with EoE; score ranges from 0 (no symptoms) to 100 points (most severe symptoms) (7-day recall period).<sup>19</sup>



<sup>§§</sup>The EoE-QoL-A questionnaire measures EoE-specific quality of life; score ranges from 0 points (perfect QoL) to 4 points (very bad QoL) (7-day recall period).<sup>20</sup>

**Table 2:** Median TSQM scores and interquartile range.

TSQM scales	PPI (n = 27); median treatment duration 6 years [3 - 9]	STC (n = 83; median treatment duration 5 years [2 - 6])	Diet (n=21; median treatment duration 2 years [1 - 4.5])
Effectiveness	66.7 [38.9 - 77.8]	83.3 [66.7 – 100.0]	77.8 [50.0 – 88.9]
Side-effects <sup>§</sup>	100.0 [100.0 – 100.0]	100.0 [100.0 – 100.0]	100.0 [100 – 100.0]
Convenience	88.9 [77.8 – 100.0]	83.3 [66.7 – 100.0]	45.8 [33.3 – 66.7]
Overall satisfaction	71.4 [50.0 -85.7]	78.6 [64.3 – 92.9]	78.6 [50.0 – 92.9]
Average score	79.9 [70.3 – 85.5]	84.8 [73.0 – 93.1]	76.6 [59.8 – 81.9]

<sup>§</sup>For a side-effect scale, a score of 100 is given to patients, who do not experience side effects.

**Abbreviations:** PPI, proton-pump inhibitor; STC, swallowed topical corticosteroids; TSQM, treatment satisfaction questionnaire for medication.

**Table 3:** Median TSQM scores and interquartile range for STC in a powdered form in patients with that therapy only as well as combined with either PPI or diets.

TSQM scales	STC only (n = 44)	STC+PPI (n = 19)	STC+Diet (n=9)
Effectiveness	83.3 [72.2 – 100.0]	77.8 [61.1 – 94.4]	83.3 [72.2 – 88.9]
Side-effects <sup>§</sup>	100 [100 – 100.0]	100.0 [87.5 – 100.0]	100 [100 – 100.0]
Convenience	77.8 [66.7 – 100.0]	83.3 [66.7 – 100.0]	94.4 [83.3 – 100.0]
Overall satisfaction	85.7 [64.3 – 92.9]	85.7 [57.1 – 96.4]	78.6 [71.4 – 85.7]

<sup>§</sup>For a side-effect scale, a score of 100 is given to patients, who do not experience side effects.

**Abbreviations:** PPI, proton-pump inhibitor; STC, swallowed topical corticosteroids; TSQM, treatment satisfaction questionnaire for medication.

386 **Table 4:** Criteria important for the choice of therapy (n=108)

	Frequency	%
Effect on symptoms	96	88.9
Effect on inflammation in the oesophagus	82	75.9
Potential side effects	75	69.4
Ease of use	63	58.3
Treating physician's recommendation	54	50.0
Compatibility with lifestyle	50	46.3
Price	21	19.4
Recommendation of other patients with this condition	12	11.1
One's own research (for example, on internet)	9	8.3
Needs of the family	5	4.6
Other Reasons	5	4.6

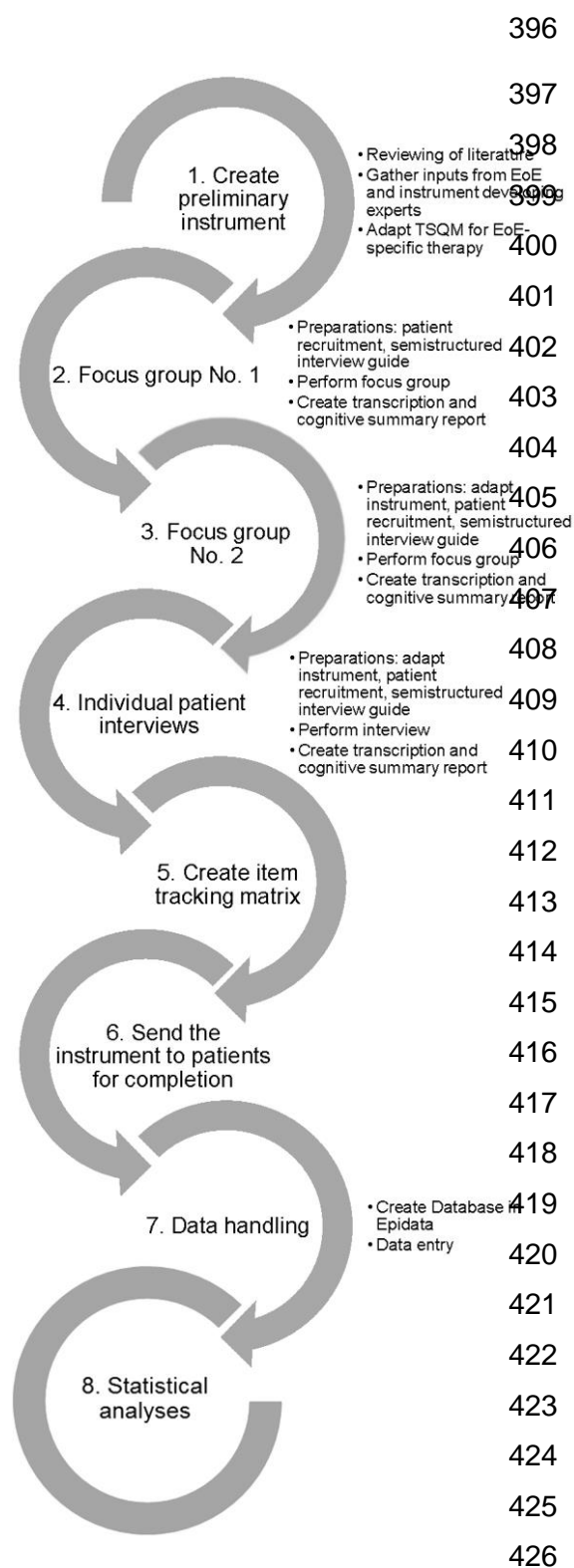
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**Table 5:** Univariable and multivariable logistic regression evaluating factors associated with assigning most importance to control of inflammation and symptoms (n=49) over control of symptoms alone (n=34).

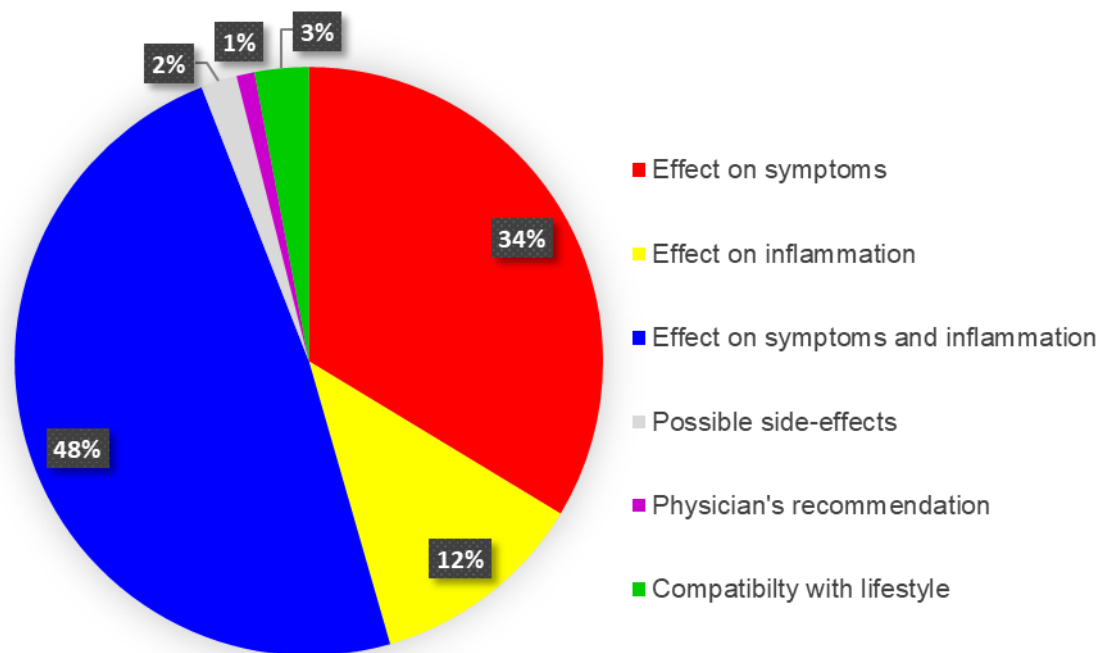
	Univariable			Multivariable		
	OR	95%-CI	P	OR	95%-CI	P
Age (years)	0.996	0.967-1.025	0.793			
Female	3.636	1.093-12.098	<b>0.035</b>	3.727	0.996-13.944	<b>0.050</b>
Disease duration (diagnosed) (years)	1.042	0.949-1.144	0.389			
Dilation (ever)	0.922	0.360-2.363	0.866			
Disimpaction (ever)	0.809	0.319-2.049	0.655			
Education level (ISCED level ≤3 vs. level ≥6)	0.390	0.156-0.971	<b>0.043</b>	0.406	0.148-1.117	0.081
STC use at the time of the study	2.451	0.863-6.963	<b>0.092</b>	3.760	1.125-12.565	<b>0.031</b>
PPI use at the time of the study	2.320	0.747-7.207	<b>0.146</b>	2.911	0.869-9.754	0.083
Elimination diet at the time of the study	0.989	0.335-2.922	0.984			

**Abbreviations:** ISCED, international standard classification of education; PPI, proton-pump inhibitors; STC, swallowed topical corticosteroids.

## FIGURES

**Figure 1:** An overview of the key steps described in the methods section.

**Figure 2:** Most important criteria for the choice of therapy.



**SUPPLEMENTARY TABLES**

**Supplementary Table 1:** Domains and items of the Treatment Satisfaction Questionnaire for Medication.

Subscale	Items
Effectiveness	1. Prevents or treats 2. Relieves symptoms 3. Time to start working
Side effects	4. Presence of side effects 5. Bothersome side effects 6. Interference with physical function 7. Interference with mental function 8. Side effects impact on satisfaction
Convenience	9. Easy to use 10. Plan when to use 11. Convenient to take
Overall satisfaction	12. Confident in benefits 13. Good outweighs the bad 14. All things into account

**Supplementary Table 2:** Application of the TSQM for EoE-specific therapy.**CONFIDENTIAL (the questionnaire is proprietary, for reviewers only)**

	Original TSQM	Diet	Dilation
<b>Effectiveness</b>	<b>Prevention or treatment</b>		
	Wie zufrieden oder unzufrieden sind Sie damit, wie gut das Medikament zur Vorbeugung oder Behandlung Ihrer Erkrankung geeignet ist?	Wie zufrieden oder unzufrieden sind Sie damit, wie gut <b>die Diät</b> zur Vorbeugung oder Behandlung Ihrer Erkrankung geeignet ist?	Wie zufrieden oder unzufrieden sind Sie damit, wie gut <b>die Dilatation</b> zur Behandlung Ihrer Erkrankung geeignet ist?
	<b>Symptom relief</b>		
	Wie zufrieden oder unzufrieden sind Sie damit, wie das Medikament Ihre Beschwerden lindert?	Wie zufrieden oder unzufrieden sind Sie damit, wie <b>die Diät</b> Ihre Beschwerden lindert?	Wie zufrieden oder unzufrieden sind Sie damit, wie <b>die Dilatation</b> Ihre Beschwerden lindert?
	<b>Time to effect</b>		
	Wie zufrieden oder unzufrieden sind Sie damit, wie lange es dauert, bis das Medikament anfängt zu wirken?	Wie zufrieden oder unzufrieden sind Sie damit, wie lange es dauerte, bis <b>die Diät angefangen hat</b> zu wirken?	Wie zufrieden oder unzufrieden sind Sie damit, wie lange es dauerte, <b>bis die Dilatation anfang</b> zu wirken?
<b>Side Effects</b>	<b>Presence of side effects</b>		
	Verspüren Sie Nebenwirkungen, weil Sie dieses Medikament nehmen?	Verspüren Sie Nebenwirkungen, weil Sie <b>diese Diät haben</b> ?	Verspüren Sie Nebenwirkungen <b>und/oder Beschwerden unmittelbar nach der Dilatation oder längerfristig</b> ?
	<b>Bothersomeness of side effects</b>		
	Wie sehr machen Ihnen die Nebenwirkungen des Medikaments zu schaffen, das Sie zur Behandlung Ihrer Erkrankung nehmen?	Wie sehr machen Ihnen die Nebenwirkungen <b>der Diät</b> zu schaffen, <b>die</b> Sie zur Behandlung Ihrer Erkrankung <b>haben</b> ?	Wie sehr machen Ihnen die Nebenwirkungen <b>der Dilatation</b> zu schaffen, die Sie zur Behandlung Ihrer Erkrankung <b>erhielten</b> ?
	<b>Interference with physical function</b>		
	Wie sehr beeinträchtigen die Nebenwirkungen Ihren körperlichen Gesundheitszustand und wie Sie im Alltag zurechtkommen (d.h. Ihre Kraft, Energie, usw.)?		
	<b>Interference with mental function</b>		
	Wie sehr wirken sich die Nebenwirkungen auf Ihren geistigen Zustand aus (d.h. auf die Fähigkeit, klar zu denken, wach zu bleiben, usw.)?		
	<b>Side effect impact on satisfaction</b>		
	Wie sehr haben sich Nebenwirkungen des Medikaments auf Ihre allgemeine Zufriedenheit mit dem Medikament ausgewirkt?	Wie sehr haben sich Nebenwirkungen <b>der Diät</b> auf Ihre allgemeine Zufriedenheit ausgewirkt?	Wie sehr haben sich Nebenwirkungen <b>der Dilatation</b> auf Ihre allgemeine Zufriedenheit ausgewirkt?

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	Original TSQM	Diet	Dilation
<b>Convenience</b>	<b>Ease of use</b>		
	Wie einfach oder schwierig ist es, das Medikament in seiner derzeitigen Form zu nehmen?	not applicable	not applicable
	<b>Planning for use of treatment</b>		
	Wie einfach oder schwierig ist es, zu planen, wann Sie das Medikament jeweils nehmen?	Wie einfach oder schwierig ist es, <b>die Menus zu planen</b> ?	not applicable
	<b>Convenience of taking medication</b>		
	Wie einfach und bequem ist es, das Medikament wie verschrieben einzunehmen?	Wie einfach und bequem ist es, <b>die Diät</b> wie verschrieben <b>einzuhalten</b> ?	not applicable
<b>Overall satisfaction</b>	<b>Confidence in benefits of treatment</b>		
	Wie überzeugt sind Sie davon, dass es gut für Sie ist, dieses Medikament zu nehmen?	Wie überzeugt sind Sie davon, dass es gut für Sie ist, <b>diese Diät</b> zu nehmen?	Wie überzeugt sind Sie davon, dass es gut für Sie ist, <b>eine Dilatation zu erhalten</b> ?
	<b>Good outweighs the bad</b>		
	Wie sicher sind Sie sich, dass die guten Seiten des Medikaments gegenüber den schlechten Seiten überwiegen?	Wie sicher sind Sie sich, dass die guten Seiten <b>der Diät</b> gegenüber den schlechten Seiten überwiegen?	Wie sicher sind Sie sich, dass die guten Seiten <b>der Dilatation</b> gegenüber den schlechten Seiten überwiegen?
	<b>All things taken into account</b>		
	Wie zufrieden oder unzufrieden sind Sie insgesamt gesehen mit diesem Medikament?	Wie zufrieden oder unzufrieden sind Sie insgesamt gesehen mit <b>der Diät</b> ?	Wie zufrieden oder unzufrieden sind Sie insgesamt gesehen <b>mit dieser Therapie</b> ?

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## REFERENCES

1. Lucendo AJ, Molina-Infante J, Arias Á, et al. Guidelines on eosinophilic esophagitis: evidence-based statements and recommendations for diagnosis and management in children and adults. *United European Gastroenterol J* 2017;5:335-358.
2. Schoepfer AM, Safroneeva E, Straumann A. Eosinophilic Esophagitis: Impact of Latest Insights into Pathophysiology on Therapeutic Strategies. *Dig Dis* 2016;34:462-468.
3. [http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/004655/human\\_med\\_002212.jsp&mid=WC0b01ac058001d124](http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/004655/human_med_002212.jsp&mid=WC0b01ac058001d124). Last accessed on August 6<sup>th</sup>, 2018.
4. Atkinson MJ, Sinha A, Hass SL, et al. Validation of a general measure of treatment satisfaction, the Treatment Satisfaction Questionnaire for Medication (TSQM), using a national panel study of chronic disease. *Health and Quality of Life Outcomes* 2004;262:12.
5. Atkinson MJ, Kumar R, Cappelleri JC, et al. Hierarchical construct validity of the treatment satisfaction questionnaire for medication (TSQM version II) among outpatient pharmacy consumers. *Value Health* 2005;8 Suppl 1:S9-S24.
6. Safroneeva E, Saner C, Rossel JB, et al. Cohort Profile: The Swiss Eosinophilic Esophagitis Cohort Study (SEECs). *Inflamm Intest Dis* 2018;2:163-170.
7. Patrick DL, Burke L, Gwaltney CJ, et al. Content validity—establishing and reporting the evidence in newly-developed patient-reported outcomes (PRO) questionnaires for medical product evaluation: ISPOR PRO good research practices task force report: Part I – eliciting concepts for a new PRO questionnaire. *Value Health* 2011;14:967–977.
8. Patrick DL, Burke L, Gwaltney CJ, et al. Content validity—establishing and reporting the evidence in newly developed patient-reported outcomes (PRO) questionnaires for medical product evaluation: ISPOR PRO good research practices task force report: Part 2—assessing respondent understanding. *Value Health* 2011;14:978–988.

9. Schoepfer AM, Straumann A, Panczak R, et al. Development and validation of a symptom-based activity index for adults with eosinophilic esophagitis. *Gastroenterology* 2014;147:1255-1266.
10. Taft TH, Kern E, Kwiatak MA, et al. The adult eosinophilic oesophagitis quality of life questionnaire: a new measure of health-related quality of life. *Aliment Pharmacol Ther* 2011;34:790-798.
11. <http://uis.unesco.org/en/topic/international-standard-classification-education-iscde>. Last accessed on August 6<sup>th</sup>, 2018.
12. Lucendo AJ, Arias Á, Molina-Infante J. Efficacy of Proton Pump Inhibitor Drugs for Inducing Clinical and Histologic Remission in Patients With Symptomatic Esophageal Eosinophilia: A Systematic Review and Meta-Analysis. *Clin Gastroenterol Hepatol* 2016;14:13-22.
13. Arias A, González-Cervera J, Tenias JM, Lucendo AJ. Efficacy of dietary interventions for inducing histologic remission in patients with eosinophilic esophagitis: a systematic review and meta-analysis. *Gastroenterology* 2014;146:1639-1648.
14. Cotton CC, Eluri S, Wolf WA, Dellon ES. Six-Food Elimination Diet and Topical Steroids are Effective for Eosinophilic Esophagitis: A Meta-Regression. *Dig Dis Sci* 2017;62:2408-2420.
15. Dellon ES, Katzka DA, Collins MH, et al. Budesonide Oral Suspension Improves Symptomatic, Endoscopic, and Histologic Parameters Compared With Placebo in Patients With Eosinophilic Esophagitis. *Gastroenterology* 2017;152:776-786.
16. Greuter T, Bussmann C, Safroneeva E, et al. Long-Term Treatment of Eosinophilic Esophagitis With Swallowed Topical Corticosteroids: Development and Evaluation of a Therapeutic Concept. *Am J Gastroenterol* 2017;112:1527-1535.
17. Greuter T, Safroneeva E, Bussmann C, et al. Maintenance Treatment of Eosinophilic Esophagitis With Swallowed Topical Steroids Alters Disease Course Over A 5-Year Follow-Up Period in Adult Patients. *Clin Gastroenterol Hepatol* 2018 Jun 11.

- 496 18. Kuchen T, Straumann A, Safroneeva E, et al. Swallowed topical corticosteroids reduce  
497 the risk for long-lasting bolus impactions in eosinophilic esophagitis. *Allergy*  
498 2014;69:1248-1254.
- 499 19. Molina-Infante J, Arias Á, Alcedo J, et al. Step-up empiric elimination diet for pediatric  
500 and adult eosinophilic esophagitis: The 2-4-6 study. *J Allergy Clin Immunol*  
501 2018;141:1365-1372.